Compilation of Articles Contributed by Experts

World AMR Awareness Week 2023
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Kerala’s AMR committees & literacy campaigns example of participatory antimicrobial stewardship

A hub-and-spoke model of AMR surveillance has been initiated in almost all districts

By Aravind Reghukumar

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Fostering patient and public engagement (PPE) to counter antimicrobial resistance (AMR) is referred to as participatory antimicrobial stewardship. PPE is recognised as an important target only in a few national policies for managing AMR.

On October 19, 2023, the World Health Organization (WHO) issued guidelines with regard to the importance of having a people-centred approach to addressing antimicrobial resistance in human health. It puts people and their needs at the centre of the AMR response and guides policymakers in taking programmatic and comprehensive actions to mitigate AMR in line with a proposed package of core interventions.

These interventions are based on a review of four pillars and two foundational steps that are critical to overcome barriers faced by people and health systems in addressing AMR. The four pillars are: (1) prevention of infections; (2) access to essential health services; (3) timely, accurate diagnosis; and (4) appropriate, quality-assured treatment.

The pillars are supported by the two foundational steps: Effective governance, awareness and education; and strategic information through surveillance and research.

The Government of Kerala realised the importance of PPE in AMR and hence during the November 2019 annual review of Kerala Antimicrobial Resistance Strategic Action Plan (KARSAP) activities by the health minister, it was decided to make Kerala an antibiotic literate / aware state.

The broad objectives envisaged under Antibiotic Literate Kerala campaign are:

1. Universal awareness about the importance of having access to antibiotic free food and water
2. Universal awareness about the importance of consuming antibiotics only on doctor’s prescription
3. Universal awareness about the importance of safely disposing unused or date expired antibiotics. For this Kerala have started a unique campaign termed Programme on Removal of Unused Drugs (PROUD) which is a joint venture of Kerala State Drugs Control Department and All Kerala Chemists and Druggists Association
4. Awareness among school students of the threat posed by AMR
5. Awareness about the importance of infection prevention and control measures like masking, hand hygiene

To make Kerala an antibiotic literate state, several initiatives have been launched by the state government, which includes preparation of online training modules on antimicrobial stewardship for doctors, AMR training modules for students, public, grassroots-level healthcare workers, pharmacists and farmers.
AMR awareness messages in the regional language (Malayalam) for the public, farmers and students have been prepared, collated and released as an AMR flip book and IEC dossier for ready reference. Public engagement through visual and print medium is routinely done.

In 2023, Kerala achieved a significant milestone by becoming the first state in India to establish AMR committees in all districts and also block-level AMR committees in all 191 health blocks. The AMR committees at district- and block-level are truly One Health-based and have representatives from the departments of health, animal husbandry, fisheries, agriculture and environment.

The antibiotic Kerala campaign is implemented through block AMR committees and is monitored by district and state AMR committees. These block AMR committees are the subdistrict bodies to disseminate the mandates on AMR programmes in the field and among healthcare professionals.

The committees also monitor AMR activities happening in each local self-government department under the block, including urban areas against the mandates of KARSAP and its goals. Monitoring and evaluation framework and standard operating procedures for block AMR committees have been issued as a Kerala government order in 2023.

The broad objectives under the Antibiotic Literate Kerala Campaign are disseminated to the public through the block AMR committees. A hub-and-spoke model of AMR surveillance has been initiated in almost all districts to facilitate diagnostic stewardship in secondary care centres.

Family Health Centre Kakkodi in Kozhikode district is set to become the first antibiotic-smart hospital in the state under the Antibiotic Literate Kerala Campaign. To be declared as antibiotic smart, just like FHC Kakkodi, a hospital should satisfy the following 10 criteria.

<table>
<thead>
<tr>
<th>MONITORING PARAMETERS</th>
<th>STATUS</th>
</tr>
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<tbody>
<tr>
<td>1. Posters on AMR in Malayalam should be displayed in hospitals</td>
<td>yes</td>
</tr>
<tr>
<td>2. All healthcare workers should be trained in infection prevention and control and antimicrobial stewardship</td>
<td>yes</td>
</tr>
<tr>
<td>3. Prescription audit must be conducted quarterly</td>
<td>yes</td>
</tr>
<tr>
<td>4. Prescription audit must be conducted quarterly</td>
<td>yes</td>
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<tr>
<td>5. IEC for public should be conducted every fortnight</td>
<td>yes</td>
</tr>
<tr>
<td>6. Antibiotic utilisation metrics with regard to dispensed antibiotics from pharmacy based on AWaRe classification should be calculated quarterly</td>
<td>yes</td>
</tr>
<tr>
<td>7. Hospital should be NQAS certified / should have a plan to work for obtaining certification in next one year</td>
<td>NQAS attained</td>
</tr>
<tr>
<td>8. Posters on AWaRe classification of antibiotics should be displayed in all prescribing areas</td>
<td>yes</td>
</tr>
<tr>
<td>9. More than 95 per cent antibiotics prescription in OPDs should be from access category</td>
<td>95 per cent is from access</td>
</tr>
<tr>
<td>10. PROUD programme or initiative for proper disposal of expired, unused antibiotics</td>
<td>yes</td>
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Aravind Raghukumar, HOD Infectious diseases, GMC Thiruvananthapuram, Kerala.
**Educating teachers and students on antimicrobial use, resistance**

Educating children on antimicrobial use instils responsible habits and attitudes early on, shaping the behaviour of future patients and caregivers.

By Sangeeta Sharma, Renu Gupta, Aditi, Vinceta Bablani, Nishtha Dang, Sandeep Bhalla

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Many of us, at some point in time, knowingly or unknowingly, have taken antibiotics without a doctor’s prescription. Reason being misconceptions about the use of antimicrobial drugs.

In our rapidly advancing world, a silent menace, Antimicrobial Resistance (AMR), is on the rise. AMR stands as a critical global health issue, worsened by the excessive use and misuse of antibiotics, particularly during the COVID-19 pandemic.

When antibiotics are not taken as prescribed or when they are used when not needed, bacteria can adapt and become resistant, making future infections harder to treat. With the diminishing effectiveness of antibiotics, our health faces a significant threat.

If AMR is not addressed urgently, we might enter a post-antibiotic era where even minor infections could become deadly which could once be treated with antibiotics, leading to prolonged illness, increased healthcare costs, and a higher risk of spreading diseases to others. It is imperative that we recognize the seriousness of this situation and unite for collective action.

Antimicrobials are recommended only for treatment of bacterial infections and most of the viral illnesses like the common cold or flu are self-limited. However, these antibiotics are sometimes over-prescribed for viral infections either themselves or on demand of patient’s leading to unnecessary prescriptions.

Additionally, individuals might self-medicate by taking leftover antimicrobials from previous prescriptions or sharing them with others, and do not complete the full course. Such practices not only fail to cure the current illness but also contribute significantly to the development of antimicrobial resistance.

Beyond human health, antimicrobials are also used in agriculture, livestock, and aquaculture, contributing to their widespread presence in the environment.

Public education on the dangers of self-medication and the importance of responsible antimicrobial use is vital in curbing this concerning trend and preserving the effectiveness of antibiotics for future generations.

Informed individuals, communities, and healthcare providers can make prudent choices, promoting judicious antibiotic use. Imagine the difference we could make if our understanding of these essential medicines started at school!
The World AMR Awareness Week (WAAW), observed every year from November 18 to 24, 2023, holds paramount importance in our global fight against AMR. The theme for this year, 'Preventing Antimicrobial Resistance Together', reaffirms the critical importance of local engagement and education in our collective efforts to combat AMR, as it did in 2022.

Schools, vital during formative years, promote health awareness and community bonds. Educating children on antimicrobial use instils responsible habits and attitudes early on, shaping the behaviour of future patients and caregivers. Informed children often influence family decisions and advocate for rational antimicrobial use, discouraging practices like self-medication.

Moreover, when teachers champion proper antibiotic usage, their impact ripples through students, parents, and the wider community, cultivating a culture of responsible antimicrobial use. Well-informed individuals grasp the risks associated with antimicrobial resistance, contributing significantly to the enhancement of public health.

This awareness helps reduce unnecessary antimicrobial requests, easing the burden on healthcare providers. Additionally, promoting proper hygiene in schools leads to fewer infections, ultimately decreasing the need for antimicrobial prescriptions.

The Delhi Society for the Prevention of Rational Use of Drugs (DSPRUD) organized mass campaigns for two consecutive years in Delhi Schools, supported by WHO, the Delhi Government, National Centre for Disease Control, and a targeted initiative with ECHO India.

In 2019, over 600,000 students from 1,000+ Delhi schools participated in the campaign. Adapting to the pandemic, the 2020 online campaign reached 3,500 teachers and 350,000 students.

In 2022, a focused three-month-long online campaign involved 180 teachers, emphasizing microorganisms, AMR, hygiene, and one-health practices.

The primary objective of these initiatives, engaging 221 schools (both public and private), was to raise awareness among school children and empower schoolteachers. By debunking myths, tackling misconceptions, and equipping educators with vital knowledge, this collaborative effort aims to shape a responsible generation that comprehends the significance of responsible antimicrobial use in safeguarding our communities against the escalating crisis of AMR.

These campaigns elevated AMR awareness, emphasizing the crucial role teachers play in shaping young minds. These teachers both in public and private schools, driven by a shared curiosity, delved into the multifaceted dimensions of AMR during the campaign.

The sessions were more than just informative; they were transformative. We navigated through the complexities of AMR, exploring the modes of transmission, emphasizing infection prevention strategies such as water and food safety, sanitation, and hygiene. Myths surrounding antibiotic usage were unravelled and highlighted the critical link between human health, animal health, and our environment.

One of the campaign’s key revelations centred around breaking the transmission chain of communicable diseases, the significance of vaccinations, the role of cleaning and disinfection, and the necessity of adhering to prescriptions. Additionally, a session was
conducted in collaboration with World Animal Protection, sensitising students about antibiotic use in animals to enhance growth and improve feed efficiency and how it enters the food chain.

Also, emphasized on the interconnectedness of human, animal, and environmental health, and the holistic ‘One Health’ approach to address this complex issue of AMR. Balancing the promotion of animal health with responsible antimicrobial use is crucial to safeguard public health and maintain a sustainable environment.

This campaign marked not just the end of a three-month journey, but the beginning of a collective mission. Educators now stand armed with knowledge, ready to empower their students with the wisdom needed to combat AMR. As we nurture a generation equipped with understanding and awareness, we pave the way for a future where antibiotics are used judiciously, ensuring a healthier, safer tomorrow for us all.

By embracing the community empowerment and responsible use, we can collectively work towards a future where antimicrobials remain effective, ensuring a healthier and safer world for generations to come.
Public health needs to be bottom line

New antibiotic research & development model required to ensure people most in need get access to right drugs

By Manica Balasegaram

Antimicrobial resistance (AMR) has been described as a silent pandemic. However, there is nothing silent about this escalating global crisis, which is now associated with nearly five million deaths a year, making it one of the world’s biggest killers.

New antibiotic treatments are urgently needed. But to stay ahead of drug-resistant bacteria, they also need to be the right antibiotics, those that have the greatest public health impact.

For that, a new antibiotic research and development (R&D) model is needed, one that ensures that the people most in need get access to these drugs, particularly in lower-income countries.

With the traditional R&D model profit, those most vulnerable have been left behind. It also is now well-known that we have seen the antibiotic pipeline dry up in recent decades, with pharmaceutical companies steadily withdrawing from the market.

But it is also why some clinically important antibiotics never got developed, because they wouldn’t be profitable enough, and it is why lower-income countries often struggle to get access to essential antibiotics, and one reason why they have the highest AMR burden. This is the public health failure at the heart of the AMR crisis.

In 2016, the organisation that I run, the Global Antibiotic Research & Development Partnership (GARDP), was created to address precisely this issue, by creating a novel public-private partnership model for antibiotic R&D that places public health needs as its central objective.

Our primary focus is the development of new antibiotic treatments that target World Health Organization priority pathogens — those multidrug-resistant bacteria that pose the greatest threats to public health — and ensuring that people in need get access to them.

Three aspects of our model, in particular, make this possible. By having an integrated R&D and access approach, we are able to factor public health constraints into the drug development process.

This means that we can make sure the end product is suitable for low-resource settings and that production costs remain low. We don’t just fund trials, we can also carry them out.

This allows us to be involved in making critical decisions, establish trial sites in regions with high prevalence of disease and recruit participants most affected by the disease that would normally be missed out, such as women, adolescents and people living with HIV.

We are also unique in our use of licensing agreements with pharmaceutical companies and manufacturers. By carrying out clinical trials and supporting regulatory submissions, these
agreements help to de-risk antibiotic drug development for donor governments supporting this work and pharmaceutical companies looking to commercialise the drug.

In exchange, we acquire the rights to manufacture and distribute treatments notably in low- and middle-income countries, making it possible for people in countries or regions of high burden to get access. Our aim is to work with a manufacturer to produce a drug that can be deployed around the world at affordable prices.

This is also partly made possible by the fact that our public-private partnership model involves working with all key stakeholders across the entire pipeline, including scientists, industry, manufacturers, regulators, donors and civil society, enabling us to make the best use of public money. Using this approach, GARDP is already making good progress towards developing five new antibiotic treatments by 2025.

Just earlier this month we announced the positive results of a phase 3 trial for zoliflodacin, a first in a new class of antibiotics, and the first to treat gonorrhoea in decades. With 82 million gonorrhoea infections each year and rising, a drug such as this couldn’t come soon enough. Resistance is growing to the last effective antibiotic treatment, particularly in Asia but now also spreading globally, so this sexually transmitted infection is now in danger of becoming one of the first diseases to no longer be treatable.

If it weren’t for this public-private model, it is unlikely that zoliflodacin would have made it this far. If it gets approved, GARDP will be licensed to distribute it to two-thirds of the world’s countries, making it available to people in lower-income countries.

Gonorrhoea is just one example. We are also working on treatments for other disease areas, such as neonatal sepsis, for which we are also seeing an alarming increase in cases that are resistant to all antibiotics. This is making it harder to treat and reversing progress on reducing neonatal mortality, particularly in lower-income countries.

In addition to developing new treatments, we are also committed to improving access to essential antibiotics that have already been approved. One reason why countries often aren’t able to get access to existing antibiotics and why they may experience shortages, is that they may be more complex to develop and manufacture and offer lower revenues than many other drugs. And yet at the same time they often have challenging regulatory requirements and smaller markets.

So, not only are fewer new antibiotics being developed, but we are also now seeing fewer existing antibiotics produced. On top of this, demand for antibiotics can often be volatile, and many countries face challenges in the management of national supplies. All this conspires to make stockouts of antibiotics much more common than for other drugs.

Through our access programme and a new joint GARDP and WHO initiative, called SECURE, we are working with countries to overcome such challenges and improve access to essential antibiotics. Part of this, for example, involves working with national regulatory authorities to see how they can help centralise the monitoring, mitigation and response to antibiotic shortages and improve market intelligence.

Further down the line, SECURE could also help to increase supply security by encouraging countries to pool procurement with other countries, which could help create more buoyant and competitive markets.
What is common to every aspect of this new public-private partnership model and why it works, is that public health is key. Because when it comes to AMR, the bottom line is that, public health needs to be the bottom line.

Manica Balasegaram is the executive director of the Global Antibiotic Research & Development Partnership (GARDP).
Antimicrobial research and development needs greater push through policies
We need policies to reward R&D, bring products to market and ensure equitable access and prudent use

By Lesley Ogilvie
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Mentioning that antibiotics are the cornerstone of modern medicine has become an integral part of anything I have written or presented since I began working in the area of antimicrobial resistance (AMR) in 2021. But if I am being 100 per cent honest with myself, I grasped the enormity of this just earlier this year, when I left a hospital in Berlin deeply grateful, relieved and hyperaware of the integral role antibiotics had played in my successful surgery for cancer.

It was a long-overdue moment of true realisation, which brought the privilege of having access to Germany’s modern healthcare facilities into sharp focus.

But I always wonder what would happen if the drugs didn’t work and the medicine cabinet was bare? This is not a thought experiment. This is a real danger for the one in five cancer patients undergoing treatment who are hospitalised with an infection — up to 8.5 per cent of cancer deaths are due to sepsis.

The World Health Organization (WHO) has been loudly sounding the alarm, making it abundantly clear that we are not developing enough new antibiotics — and other antibacterials — to deal with the growing tide of AMR, especially the most dangerous resistant bacteria causing severe infections like pneumonia, bloodstream infections or meningitis.

The World Antimicrobial Resistance Awareness Week takes place from November 18-24 every year.

There are thousands of oncology drugs currently in clinical development, compared with just 77 antibacterials. This is despite the fact that patients taking cancer treatments are reliant on working antibiotics to avoid life-threatening infections.

There is a growing body of work outlining the unique challenges facing developers of antibiotics, namely the high cost of research and a low return on investment, with experts and stakeholders alike calling for a change in policy and perspectives that would create a more sustainable innovation ecosystem.

AMR is not a secret. It’s been high on political agendas for a number of years, with commitments for action forthcoming, including across the United Nations, Group of Seven (G7), Group of 20 (G20) and European Union.

Since the first UN General Assembly (UNGA) declaration on AMR in 2016, which represented a major milestone for political action against AMR, a number of initiatives have been created to help advance this agenda. This includes the creation of public-private partnerships such as CARB-X and GARDP, as well as the organisation I work for — the Global AMR R&D Hub.
Global AMR R&D Hub was formed in 2018 following a G20 call in 2017 for “a new international R&D Collaboration Hub to maximise impact of existing and new anti-microbial basic and clinical research initiatives as well as product development”. There was a clear recognition that research is a crucial feature of our toolkit to combat AMR globally, but that we need an evidence base to help support decision making, especially with finite funds and many competing global challenges.

The Hub’s Dynamic Dashboard collects data on public and philanthropic funding for AMR research and development (R&D) across all One Health sectors, as well as information on global incentives to improve the antibacterial R&D ecosystem and market functioning.

So, there have been major international and national programmes and global partnerships established to encourage antibiotic and antibacterial R&D. CARB-X and GARDP are great examples of such partnerships with a focus on the most critical public health needs, helping to bolster those fragile preclinical and clinical pipelines.

But it’s not enough. It is widely recognised that we need both push and pull — or other innovative — policies working together, to reward R&D, bring products to market, and ensure their equitable access and prudent use.

The UK’s antibiotic subscription model, which pays for the ability to access the drug, not the volumes used, is one way forward. The United States, Canada and Japan are all considering versions of these financing mechanisms at the moment, but more co-ordinated action is required.

This year’s World AMR Awareness Week theme, Preventing antimicrobial resistance together, also highlights the need for AMR to be tackled at multiple levels across many different sectors. The development of AMR vaccines and diagnostics continues to be underfunded; these receive three times less funding than therapeutics. We are still failing to connect the dots across the One Health spectrum.

Although the use of antimicrobials in the animal sector vastly exceeds their use in human health, only about 8 per cent of the recorded R&D funding in our database involves animal health. The environmental and plant health sectors receive a fraction of this. Only 6 per cent of all funding is being invested in cross-sectoral projects – those that involve more than One Health sector – but R&D funding has been increasing, doubling since 2017.

The focus is now on contextualising this data to help policymakers and funders further co-ordinate and prioritise R&D activities to ensure impact.

The upcoming UNGA high level meeting on AMR in September 2024 provides an opportunity to accelerate action and accountability on AMR and strengthen the R&D ecosystem for it across the One Health spectrum. This includes targeted and aligned action on both push and pull, through sustainable and predictable financing and resources, and the setting and monitoring of R&D targets for the development of those key health technologies (for example, therapeutics, diagnostics and vaccines) that we need to address the most critical public health needs.

It’s a lot, but it’s doable. We just have to keep doing better together.

Lesley Ogilvie is director of the secretariat, Global AMR R&D Hub, Berlin, Germany
Innovation in antibiotics research and development is urgently needed

There should be a movement to treat AMR as a national issue, pass policies and fund innovation. Such efforts would then have a cascading effect and allow funding to pour in from private investors

By Vasanthi Ramachandran

Antimicrobial resistance (AMR) is now recognised as an imminent health crisis ranked among the top 10 global threats affecting humanity. Most infections have now become untreatable owing to the emergence of “superbugs”. The looming danger of drug-resistant infections, the so-called “silent pandemic”, has thrown up major challenges for the healthcare sector warranting immediate action on a war-footing to curb this menace.

The discovery of penicillin was viewed as a much-needed remedy for the control of infections that were otherwise leaving humans with debilitating outcomes and high mortality rates. Antibiotics were considered as a huge blessing, providing the much-needed relief to humanity’s infection wreaked sufferings.

Surprisingly, Alexander Fleming had aptly warned of a clear possibility of antibiotic resistance following repeated use within society. A few decades later, multiple new antibiotics developed at a steady pace, with varying mechanisms of action. However, beyond the 1970s, there was a lull due to which the current antibiotic pipeline has run dry.

Looking back at what led to this dire situation, there seem to be a few obvious key indicators. There has been severe overuse, misuse, or abuse of antibiotics.

Shockingly, the rampant usage in livestock and agriculture compounded with inefficient waste management processes have led to adverse impact on the environment, including soil or aquatic systems which have now become extensively contaminated with drug-resistant bacteria.

On multiple fronts, the trajectory of antibiotic discovery has not taken off as expected.

It has been observed that there is lack of innovation in the area of AMR. Innovation through identification of new chemical classes with novel mechanism of action, possibly hitting more than one target may succeed in delaying resistance development.

However, target-based approaches have met with very little success as most of these pre-clinical candidates failed to show cellular activities due to either poor permeability or efflux liabilities.

Cell-based approaches, while succeeding in translating to cellular activities, do have to go past toxicity-related hurdles to qualify for the next stage and progress further into clinical development.

To add to the already difficult circumstances, most big pharma companies have exited this arena. A short course of antibiotic therapy meant less profitable returns unlike therapies for cancer or chronic life-style diseases which guarantees a major market share, often needing usage for an entire lifetime.
Recently, a slew of Public-Private-Partnerships have come forward and provided the necessary stimuli via grants and other support to facilitate discovery efforts and enable clinical development. These efforts — labelled as “push incentives” — need to be adequately complemented with ‘pull’ incentives, which guarantees revenue and sustenance to the antibiotic developers irrespective of the drug sales.

Current antibiotic discovery explorations have now shifted from big pharma to SMEs, a paradigm shift which while offering opportunities to innovate, allowing operations via flexible working models with quicker decision-making and rapid course correction options, need timely funding and support as research and development (R&D) explorations are risky and costs are quite prohibitive.

Other major hurdles that antibiotic innovators have to overcome, is the “science”, as it is extremely hard to identify new druggable targets for designing antibacterials.

Secondly, regulatory paradigms are tough to fulfil as high dosages are required for treating infections even if the duration is short. Thus, safety margins may prove to be quite difficult to achieve.

Thirdly, there are very limited funding options, and no private investment is available for clinical development. It’s a tough ask to keep the company afloat, without completely diluting and still have some ownership and equity.

Finally, market forces are poorly organised. Even after you bring out the best molecule with half a billion dollar investment, there is no assurance of revenue for the company. For such a scenario, the government should step forward to pay for value and not by volume.

Another important issue which is specifically linked to antibiotics is that even if efforts are directed for optimal and affordable drug access to patients, we need to ensure that there is no overuse to avoid resistance development.

As far as potential solutions are concerned, it would be beneficial for all major regulatory bodies to come together, treat AMR challenge as equivalent to the climate change problem. They should, as a combined force, work in a harmonised manner with a common agenda to support clinical trials, minimise duplication and lessen the burden on the developers without compromising safety.

Any enterprise which is seriously pursuing to solve AMR issues especially in a country like ours wherein the burden is very high, adequate support by the government is needed via funding for R & D, infrastructure and clinical development and provide incentives.

There should be a movement to treat AMR as a national issue, pass policies and fund innovation. Such efforts would then have a cascading effect and allow funding to pour in from private investors.

As a start-up, we feel we have strived hard to achieve a near impossible feat. We could assemble a global team with expertise in this area along with global suppliers, collaborators, investors etc, towards identifying a broad spectrum antibiotic after nearly 60 years and provide a one-stop solution for public health, war-fighter health and biothreats.

We took upon the challenge of AMR, a global health issue in India. As it is obvious, the R & D path for tackling AMR is very long and arduous. We feel that the areas to improve upon
include a better understanding of some of the nuances of clinical development and for a sustainable working model, find quicker ways to close deals.

As the over-arching goal to resolve the AMR crisis, “One Health” is viewed as a unifying multi-disciplinary solution wherein we ensure a safe ecosystem and optimal health for all life forms.

Such an initiative includes stewardship encompassing regulated antibiotic usage, surveillance, infection control and also extend measures to incentivise innovation of novel antimicrobial discovery along with alternatives to antimicrobials for non-human use.

Save humanity globally from this alarming health threat of AMR now.

Vasanthi Ramachandran is Vice President – Collaborations in Bugworks Research India Pvt. Ltd and involved in leading efforts in Clinical Microbiology and external Collaborations within India and worldwide for both pre-clinical studies and clinical development
India poised to advance in antibiotic development: VS Chauhan & Nitin Yadav

CSE-DTE speak to Virander S Chauhan and Nitin Yadav, co-founders of Biotide Solutions LLP, about the global AMR scenario

By Neeraj Kumar
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Virander S Chauhan and Nitin Yadav are co-founders of Biotide Solutions LLP, a startup company working towards developing novel antimicrobials for multi-drug resistant bacterial infections. Centre for Science and Environment-Down To Earth spoke to the duo during the recently observed World Antimicrobial Awareness Week 2023. Edited excerpts:

Neeraj Kumar (NK): What is the current global situation of antibiotic drug development?

VS Chauhan (VSC) & Nitin Yadav (NY): The current global scenario of antibiotic drug development is indeed facing a critical crisis. There is a distressing scarcity of novel antibiotics entering the market, leading to a serious threat in addressing increasingly resistant infections.

It is concerning that despite the significant challenge of antimicrobial resistance (AMR), the number of drugs in development addressing this issue remains notably low.

Currently, only 77 antimicrobial therapeutics are in clinical trials, with 32 as non-traditional antibiotics, compared to around 10,000 drugs for cancer and 1,800 for neuropsychiatric diseases.

Several factors contribute to this situation, encompassing the rapid acquisition of resistance by bacteria against antibiotics, the exorbitant costs linked with drug development, the extensive duration needed to bring a new drug to market, and the insufficient financial incentives provided to pharmaceutical companies.

NK: How does current global antibiotic development situation impact Indian industry?

VSC & NY: The Indian pharmaceutical industry holds substantial potential to play a prominent role in advancing new antibiotics. With its successful history in manufacturing high-quality yet low-cost generic drugs, the Indian pharmaceutical industry possesses all the necessary capabilities to develop various new drugs, especially antibiotics, which will need large-scale production to meet global demands.

Moreover, the industry has easy access to a large pool of workforce including skilled scientists and researchers.

However, the Indian pharmaceutical industry faces several obstacles, such as significant expenses related to drug development, limited financial incentives and the need for improved regulatory frameworks. Addressing these challenges is crucial to unlocking the full potential of the Indian pharmaceutical sector in driving the development of new antibiotics.

NK: What are some of the challenges & limitations faced by Indian drug developers?
VSC & NY: Indian antibiotic drug developers face several challenges in their efforts to develop new antibiotics. Some of these challenges include:

**Scientific and technological barriers:** Developing new antibiotics demands advanced scientific research employing innovative drug discovery approaches and a deep understanding of complex mechanisms underlying bacterial resistance. However, India faces obstacles here due to limited scientific infrastructure, absence of specialised expertise and gaps in technological capabilities, hampering the advancement of antibiotic drug development.

**Funding constraints:** Antibiotic research and development require urgent attention in terms of long-term focused funding, which is usually not available to researchers in scientific institutes. Additionally, the high cost of research and development, coupled with the uncertain return on investment, poses financial limitations for drug developers.

**Collaborations and partnerships:** Collaboration among academia, industry and government entities is crucial for antibiotic drug development. However, establishing effective collaborations and partnerships, aligning research goals, sharing resources, and fostering a collaborative environment poses challenges due to logistical, regulatory, and competitive factors.

**Market competition:** In the landscape of research and development of novel antimicrobial therapeutics, intense global competition, particularly within the generic drug market, poses a significant challenge for Indian companies. Balancing investments in innovative research and maintaining competitive pricing becomes notably difficult due to this competition.

NK: How can the challenges faced by the Indian antibiotic development industry be addressed?

VSC & NY: Here are some specific ways in which the challenges faced by the Indian antibiotic drug development industry can be addressed:

**Research and development investments:** Long-term focused funding in research and development (R&D) is crucial for both academia and the Indian industry to bolster their antibiotic drug development capabilities. The allocation of resources toward exploring new compounds, identifying novel drug targets, and pursuing innovative treatment approaches holds significant promise in discovering novel antibiotics.

**Collaboration and partnerships:** Collaboration involving academia, government institutions, and pharmaceutical companies is crucial for sharing knowledge, expertise, and resources. It is essential that academia, industry, and government agencies collaborate closely to tackle the complexities in developing new antibiotics. Creating partnerships between clinicians and research scientists in labs is vital, as it speeds up antibiotic development by combining the strengths and expertise of different groups.

**Regulatory support:** Creating streamlined regulatory frameworks designed specifically for antibiotic drug development has the potential to speed up the approval process, ensuring strict compliance with safety and efficacy standards. Clear guidelines and strong support from regulatory bodies can incentivise the Indian industry to invest more in antibiotic research and development efforts.

**Antibiotic stewardship programs:** Establishing antibiotic stewardship programs within healthcare settings is crucial for promoting responsible antibiotic use, preventing misuse,
and reducing the emergence of resistance. These initiatives substantially contribute to conserving the efficacy of both existing and any new antimicrobial drugs, enhancing their utility, and confronting the challenge of antimicrobial resistance.

**Global collaborations:** Partnering with international organisations, research institutes, and pharmaceutical companies provides access to expertise, resources, and funding opportunities. Engaging in global research consortia and clinical trials can significantly bolster the Indian industry’s involvement and contributions to antibiotic drug development.

**NK: What are some efforts or initiatives that have been taken to promote antibiotic R&D in India?**

**VSC & NY:** While India has made notable contributions to antibiotic research, there is a need for increased focus on developing new classes of antimicrobial therapeutics to combat the growing threat of antimicrobial resistance.

To address this, the Indian government has taken steps to promote antibiotic research and development. Initiatives like the National Antimicrobial Resistance Strategy have been implemented to strengthen R&D efforts and enhance collaborations between academia, industry, and government bodies.

Financial support, regulatory reforms and capacity-building initiatives are being pursued to foster a conducive environment for antibiotic development in India.

While there is room for growth and improvement, India’s position in antibiotic development is poised for advancement. With its strong pharmaceutical industry, research capabilities, and ongoing initiatives, India has the potential to play a significant role in addressing the global challenge of antimicrobial resistance through the development of novel effective antibiotics.

Finally, India can and should play a leading role in the fight against AMR, as it addresses a major health challenge not only in India but also in the Southeast Asian countries.
Subscription-based economic model can help unblock pipeline for new antibiotics

At present, drug development is only profitable if combination of prices and sales volumes is sufficiently high

By Laurence Roope
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The World Antimicrobial Resistance Awareness Week takes place from November 18-24 every year.

Bacterial infections are becoming increasingly resistant to our stock of antibiotics, and unfortunately, the pipeline for new types of antibiotics is blocked. The reason for this blockage has as much to do with economics as with hard science. Without the right incentives, drug companies are unlikely to develop the new antibiotics that are so badly needed.

The revenue that companies make from new drugs, including antibiotics, depends on the volumes they sell and at what prices. Drug development is expensive and so it is only profitable if the combination of prices and sales volumes is sufficiently high.

Unlike most other drugs, once an effective new antibiotic is developed, there is a need to restrict its use so that bacteria do not quickly become resistant to it. This reduces the volumes that are likely to be sold, often to the point where antibiotic development can be loss making. In sum, the traditional economic model does not provide good incentives for companies to develop novel antibiotics.

How can we fix the model

It is widely agreed that two things are needed. First, state interventions that reduce the cost of research and development (R&D), such as research grants and tax credits, are needed. However, this alone is not enough. We also need incentives that provide assurance to companies that, once they manage to develop safe and effective new antibiotics, they will receive sufficient rewards.

Because of the pressure to restrict the use of new antibiotics, the rewards offered need to be “delinked” from sales prices and volumes. There have been small positive developments in this direction. In the United Kingdom, for example, the government has been testing a subscription model, where annual lump-sum payments are made for two existing antibiotics.

The size of these payments is based on analyses of their value to the UK National Health Service, in terms of their overall health benefit, rather than on the number of doses that are sold. This approach has been dubbed the “Netflix model” – for a fixed subscription rate, the buyer is entitled to use the antibiotics as much as they want, while the supplier is guaranteed a steady income stream.

Even so, progress remains very slow. This is partly because it is difficult to estimate the value of new antibiotics and therefore, how much the subscription fee should be. Estimating the value of antibiotics is difficult compared to other drugs.
With other new drugs, it is relatively easy to evaluate how much health benefit they provide compared to existing drugs. If they are only equally effective as older drugs then, unless they cost less or the older drugs are difficult to supply, their value will be limited.

In contrast, new antibiotics are likely to be very valuable, even if they are no more effective than current antibiotics. This is because, over time, bacteria are likely to develop further resistance to our current antibiotics. Much of the value of the new antibiotic may come from the options it provides us in the future, if it remains effective when current antibiotics become less so.

However, evaluation is not the biggest obstacle. As the UK pilot has shown, well-designed analyses can provide useful, pragmatic estimates of antibiotic value. The biggest barrier to fixing the broken economic model is finding and coordinating countries or institutions that are willing to pay the sums that are needed.

Making the development of a novel antibiotic profitable is estimated to cost somewhere in the region of $3 billion. To put this number in context, the current subscription scheme in the UK pilot provides only £100 million (approximately $125 million) over a 10-year period. Significant global coordination is likely to provide the funding needed for incentivising the development of completely new antibiotics.

One proposed approach to co-ordination is the Health Impact Fund (HIF). This would be a government-funded agency that offers annual rewards pools, from which new drugs would receive a share. The share that each drug would receive would be based on an evaluation of the drug’s overall impact on global health.

Those drugs that contribute most to global health would receive the greatest rewards from the pool. In this way, firms would be rewarded according to the health impact of their drugs rather than the volumes they sell. In fact, part of the idea is that the firms would be obliged to sell their drugs at or below cost price — so that their remuneration would be purely value-based.

Countries could contribute a certain percentage of their gross domestic product (GDP) to the HIF. If enough countries got involved, only a very small share of GDP would be needed to create a fund big enough to make a major contribution to unblocking the antibiotic pipeline.

The HIF could also go a long way towards overcoming barriers to the development of other drugs that the market currently underfunds, most notably those for so-called diseases of the poor like tuberculosis and malaria.

As with tackling the climate crisis, significant investment in innovation must also be a major part of the solution to the antibiotic resistance crisis. However, in addressing both of these major issues, we must not lose sight of the importance of conserving the precious resources we currently have in the hope of new technology.

Just like extreme inequality in carbon footprints across and within countries, the excess use of antibiotics co-exists with a lack of access to essential lifesaving antibiotics. Finding ways to optimise the use of antibiotics, ensuring that they are used where they should be, and not used when they should not be, must also be an important focus for public policy.

Laurence Roope is a senior researcher at the Health Economics Research Centre (HERC), part of the Nuffield Department of Population Health at the University of Oxford.
Tackling antimicrobial resistance is a critical global function

By Gavin Yamey
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The devastation caused by the COVID-19 pandemic has finally, and belatedly, forced the global health community to recognise that it has been neglecting an array of international collective action for health (ICAH) activities, including pandemic preparedness and response.

In 2020 and 2021, there were 14.83 million excess deaths globally associated with the pandemic, the WHO estimated. The pandemic will cause $13.8 trillion in economic losses by the end of 2024, according to the IMF.

These eye-watering numbers show the enormous costs of inaction when it comes to preparing for and tackling threats that transcend the boundaries of nation states, like pandemics, climate change and the global spread of antimicrobial resistance (AMR).

The world should have taken heed after the 2014-2016 Ebola epidemic in West Africa, which took a very long time to control. While it is true that weak national health systems in Guinea, Liberia and Sierra Leone made it harder to bring the epidemic to an end, another critical reason for the prolonged epidemic was the neglect of ICAH.

When the epidemic began, there was no Ebola vaccine, treatment or rapid diagnostic test, reflecting insufficient funding for and attention to research and development for emerging infections; regional surveillance systems performed poorly; and the WHO was criticised for its weak governance and leadership, which itself was due to a budget crisis.

It is clear that the world has largely been neglecting the need to finance, organise, govern and deliver a critical set of ICAH activities. Funding for such activities tends to rise after a crisis — as it did after the 2014-2016 epidemic — but then falls again once the crisis recedes, a pattern that is known as “cycles of panic and neglect”.

A key question for the future of global health is: How can these cycles be broken? How best can the case be made for sustained attention to ICAH activities?

One strategy that has emerged is advocacy for aid donors and all nations to invest more in global public goods (GPG). While this is a welcome strategy, it comes with an important limitation: The narrow definition of a public good.

The conventional definition of a public good is one that is non-rival (if one person consumes it, this does not reduce its availability to others) and non-excludable (no one can be denied access). Examples of GPGs for health include an open access research publication or a patent on a new antimicrobial drug, provided the patent is shared in the Medicines Patent Pool.

However, as my colleagues and I previously argued, the problem with using such a narrow definition is that it is “inadequate to capture the broad array of international collective actions needed to address supranational health challenges”.

Tackling AMR or climate change, improving the surveillance of infectious diseases and strengthening the WHO’s core functions are all ICAH activities that go far beyond GPGs alone.

The narrowness of the public goods definition is a key reason why the WHO came up with a new term, “common goods for health (CGH)”, which, they say is, “a new construct born out of the observed failures exposed by Ebola, SARS, Zika, and other communicable diseases as well as by other health and environmental risk factors.”

The term CGH includes GPGs but goes beyond them to also include goods or services that have “large social externalities, and thus will not arise through market forces alone”.

The *Lancet* Commission on Investing in Health went even further, coining the term “global functions”, which has three categories: GPGs; management of cross-border regional or global externalities (spillover harms and costs that are suffered by a third party and that go beyond nation state boundaries, such as AMR, pollution or pandemics); and fostering global health leadership and stewardship.

There are many advantages to using a global functions framework rather than just the narrow public goods framework. First, a global functions framework helps to clarify, define and classify essential ICAH activities. Second, when it comes to monitoring how much finance is being directed at ICAH, and how much additional funding is needed, a global functions framework helps the international health community to know what it is that we are prioritising, how much we are spending, what the price tag is, and the size of the funding gap (the gap between what we are spending and the amount needed).

Methods and tools are now available for tracking funding for ICAH activities. Finally, “global functions” capture the *broad array* of transnational activities that are critical in preparing for and responding to transnational challenges, including AMR.

<p>| Lancet Commission on investing in health’s classification of global functions |</p>
<table>
<thead>
<tr>
<th>Global function</th>
<th>Examples</th>
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| Supplying global public goods | • Research and development for health tools  
• Development of norms, standards and guidelines  
• Knowledge generation and sharing  
• Intellectual property sharing  
• Market-shaping activities |
| Managing cross-border externalities | • Outbreak preparedness and response  
• Responses to antimicrobial resistance  
• Responses to marketing of unhealthful products  
• Control of cross-border disease movement |
| Exercising leadership & stewardship | • Health advocacy and priority setting  
• Promotion of aid effectiveness and accountability |

The World Antimicrobial Resistance Awareness Week takes place from November 18-24 every year. *Gavin Yamey is the director of the Center for Policy Impact in Global Health, Duke Global Health Institute, US*
How colistin went from 'holy water' in medicine to 'sewage' of resistance

More research is needed to find out the long-term effects of using colistin on humans

By Abdul Ghafur

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The rise of resistance to the antibiotic colistin represents a formidable threat to global public health. Colistin, which is sometimes called an “antibiotic of last resort”, is very important for treating serious infections caused by gram-negative bacteria that are very resistant to many drugs. In clinical settings, we treat colistin with the highest level of caution, reserving its use for cases where other antibiotics have failed.

However, the recent global rise in colistin resistance, particularly due to the spread of the mobilised colistin resistance gene, is alarming. This gene is often found on the mobile genetic elements of bacteria that live in livestock. It has been linked to the widespread use of colistin in agriculture, especially as a way to help plants grow. When these resistance genes jump from animals to humans, they can lead to treatment failures.

The World Antimicrobial Resistance Awareness Week takes place from November 18-24 every year.

The use of antibiotics to promote growth in livestock is a practice where sub-therapeutic doses of antibiotics are administered to healthy animals, which can also improve feed efficiency. While this practice has been beneficial for increasing production in the agricultural industry, it has also been widespread, particularly in intensive farming operations.

The antibiotics used for growth promotion are often the same or belong to the same classes as those used to treat human infections. This extensive use has led to a selection pressure that favours the survival and spread of antibiotic-resistant bacteria, which can be transmitted from animals to humans through direct contact, the environment and the consumption of contaminated food products.

The practise of using antibiotics for promoting growth is of great concern because it accounts for a significant portion of antibiotic use globally and poses a direct threat to human health by reducing the effectiveness of critical antibiotics.

In India, prior to 2018, the prevalence of colistin-resistant bacteria in the agricultural sector was not well documented. Recognising the dire implications of this knowledge gap, our interdisciplinary team of doctors and scientists embarked on a pivotal study.

We tested poultry, fish, and vegetable samples for colistin-resistant bacteria and found a disturbingly high incidence. Findings from our study showed that the colistin-resistant genes in these samples were caused by using the antibiotic to help poultry grow.

The study extended to a group of young, healthy volunteers, among whom 14 per cent were found to be carriers of colistin-resistant bacteria in their gut flora. Genomic analyses confirmed that these bacteria were not of hospital origin but were associated with the same strains found in poultry.
The implementation of the ban on the commercial use of colistin for growth in 2019 marked a significant milestone in the fight against antibiotic resistance in India. This move has markedly curtailed the use of colistin as a growth promoter in the poultry industry. Still, we need to stay alert and do more research to find out what the long-term effects of using colistin and the resistance patterns among human populations.

The Chennai Declaration, an initiative aimed at curbing antibiotic resistance, played an instrumental role in bringing about this legislative change. Persistent efforts of the Chennai Declaration team, active engagement with policymakers and interdisciplinary work of relevant ministries of the central government were crucial in achieving the prohibition of colistin for growth promotion.

Looking forward, India’s commitment to antibiotic stewardship must extend beyond colistin, encompassing a range of medically important antibiotics that are still used as growth promoters. Continuing research, surveillance, and policy advocacy are critical to ensuring that the positive steps taken are reflected in reduced resistance rates and the protection of public health.

With its vast resources and intellectual capital, India is well-positioned to lead the development of sustainable practices in animal husbandry that do not compromise human health.

*Abdul Ghafur is coordinator, Chennai Declaration and consultant in infectious diseases, Apollo Hospital, Chennai*
US FDA is too close to meat and drug industries when it comes to protecting public health

FDA has helped to create antibiotic-intensive livestock system of US

By Steve Roach
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The United States is the world’s third largest consumer of antibiotics for animal agriculture. Most of the use is in the highly concentrated pig and cattle sectors. Just 3,600 swine-raising facilities produce 73 per cent of the over 235 million pigs produced in the US each year. Less than 600 operations produce 75 per cent of all US feedlot cattle.

These enormous livestock facilities, raising tens of thousands of animals, routinely feed antibiotics to counter unhealthy conditions and practices. The end result is high antibiotic use. For example, US pig producers use about three times as much antibiotics to raise a pig as pig producers in the United Kingdom. US cattle producers use about five times as much antibiotics as producers in Denmark.

However, there is one bright spot when it comes to antibiotic use in US animal agriculture. Over ten years ago, the chicken industry started competing as to who could raise chickens with fewer antibiotics. The end result is that most chickens raised in the US do not receive antibiotics that are in the same classes as antibiotics used in human medicine.

The US Food and Drug Administration (FDA) has, for the most part, helped to create the antibiotic-intensive livestock system that dominates US animal agriculture. The FDA is tasked with reviewing antibiotics before approval for use in animals to make sure they are safe and effective. While the Agency has at times taken steps to restrict antibiotic overuse, its day-to-day operations are aimed at approving new drugs and making them available to livestock producers. The World Antimicrobial Resistance Awareness Week takes place from November 18-24 every year.

Once drugs are on the market, the FDA struggles to address newly identified safety problems, even when these safety issues are very apparent. The FDA has failed to create indicators that could be used to measure its progress on addressing antibiotic resistance, has aided the creation of a livestock industry that relies on regular and routine use of antibiotics in feed and water to compensate for unhealthy living conditions, and has failed to implement even the most basic monitoring of how and why antibiotics are raised in food animal production.

The FDA has taken some — very limited — steps to address these issues. In the 1970s, after the problem of antibiotic resistance from the overuse of antibiotics in livestock became apparent, it started requiring drug makers to submit tests showing their products would not create a resistance problem if they were going to be used in feed for more than 14 days.
This resulted in some feed additives having a 14-day duration limit, which likely has helped limit some overuse. The FDA also at that time tried to withdraw approvals for feed uses of penicillin and tetracyclines, but never followed through.

Decades later in 2003, the FDA began requiring new antibiotic approvals for use in animals to be evaluated to see if they created a risk of resistance. During the discussion about the new approach the FDA stated they intended to look at old approvals as well. They did this for a few drugs, but when the results came back that some of the old approvals failed evaluations, the FDA notified the companies and then did nothing else.

In 2005, the FDA banned the use of the critically important class of drugs fluoroquinolones for use poultry when evidence showed its use was making it harder to treat foodborne infections. The result is lower levels of resistance to fluoroquinolones in US poultry than in most other countries. In 2008, the US legislature required the FDA to begin collecting and reporting data on sales of antibiotics for use in animals.

This was a big step forward and it was improved over time by requiring the drug makers to estimate what species were receiving the drugs. Still, the sales data fail to provide information on why antibiotics are used and do not distinguish types of production such as laying chickens versus chickens raised for meat.

Finally, in 2017 the FDA completed a plan that prohibits the use of medically important antibiotics for growth promotion. This led to a 43 per cent drop in sales of medically important antibiotics, but sales have gone up since then.

The US and US FDA still fail to follow important international expert recommendations on reducing the risk of antibiotic resistance in the food system. First, the US has failed to put in place any indicators to measure progress of its efforts to address the antibiotic resistance crisis. The US should follow the example of countries that signed the Muscat Manifesto to set targets for reduction in antibiotic use in agriculture.

So far, the FDA and other US government agencies have rejected any calls for reducing antibiotic use in agriculture and have instead only been willing to discuss reducing the need for antibiotics, essentially assuming that current use is needed. The US has also failed to create any indicators of resistance in bacteria in the food system.

The US does not follow international recommendations to eliminate or restrict the use of antibiotics for disease prevention. Restricting the preventive use of antibiotics is a recommendation of the World Health Organization Guidelines on the use of Medically Important Antibiotics in Animals.

The US has also not implemented the Codex Alimentarius Code of Practice that states that preventive use of medically important antibiotics should only be used under "exceptional circumstances." In US cattle and swine, use of preventive antibiotics is routine and completely unexceptional. Instead of eliminating routine preventive use the FDA has decided it will address continuous use of antibiotics in animal feed.

Currently about a third of approvals for medically important antibiotics in feed can legally be fed continuously with no duration limit. The FDA has indicated it wants to add duration limits to all medically important drugs, but its current draft proposal suggests any duration shorter than the whole life of the animal will likely be acceptable.
The US FDA has also failed to put in place international recommendations to collect information on how antibiotics are used in food-production. The Agency is currently exploring a voluntary public-private partnership which will give the animal production industry complete control over how the data will be collected and reported.

Like so many of the actions of the FDA related to antibiotic resistance, such as its efforts to create duration limits, its data collection proposal prioritises the needs of the regulated industry over public health. The Agency has so far ignored calls from public health advocates to collect data on antibiotics delivered to livestock feeding operations in animals, despite having the legal authority to collect this data.

Sadly, despite a consensus that antimicrobial resistance is a critical global health crisis, actions that inconvenience the giant US meat industry are not considered.

*Steven Roach, MA is the Safe & Healthy Food Program Director at Food Animal Concerns Trust*
**Tackling antimicrobial resistance in agrifood systems through a One Health approach**

Adopting a whole-of-society and multi-sectoral approach is essential to address AMR effectively

By Junxia Song, Alejandro Dorado García, Emmanuel Kabali, Yu Qiu, Nelea Motriuc, Fallon Bwatu Mbuyi

Antimicrobial resistance (AMR) is a major global threat to humans, animals, plants and the environment. The Food and Agriculture Organization (FAO) of the United Nations plays a pivotal role in facilitating responsible antimicrobial use in the food and agriculture sector. By collaborating with governments, producers, traders and various stakeholders, FAO actively contributes to increasing capacities in managing AMR and building resilience to its impacts in agrifood systems.

As a multidisciplinary organisation, FAO leads the global response to AMR in the food and agriculture sectors. Its work, currently guided by the FAO Action Plan on Antimicrobial Resistance 2021-2025, aims to address the various challenges AMR poses. This action plan sets out the five objectives that guide the programming of FAO activities:

1. Increasing stakeholder awareness and engagement
2. Strengthening surveillance and research
3. Enabling good practices
4. Promoting responsible use of antimicrobials
5. Strengthening governance and allocating resources sustainably

The FAO Action Plan is designed to support the Global Action Plan on AMR, emphasising a coordinated and multi-sectoral One Health response. This approach acknowledges the interconnectedness of human, animal, plant and environmental health.


The partnership addresses shared challenges and opportunities in addressing AMR across various policy and technical areas.

**Strengthening surveillance**

To bolster a country's capacity for surveillance and monitoring of antimicrobial resistance and use in food and agriculture, FAO advocates for a standardised approach to data collection, analysis, interpretation and sharing.

Despite worldwide initiatives generating AMR surveillance data, challenges persist due to insufficient data management systems, unclear roles and responsibilities in data reporting and a shortage of trained experts for analysis and interpretation.
In response, FAO committed to establishing a comprehensive global epidemiological information system for regularly collecting and analysing reliable and comparable data on AMR within the food and agriculture sectors.

In pursuit of this commitment, FAO embarked on the development of the International FAO Antimicrobial Resistance Monitoring (InFARM) System. As of December 2022, FAO has successfully completed the development of a beta version of the InFARM IT platform, which was subsequently made available for pilot testing in a select number of countries until March 2023.

During this pilot phase, users have provided invaluable feedback, which FAO actively incorporates into the final stages of IT development. In anticipation of the following steps, FAO plans to launch a global call for AMR data in the first quarter of 2024.

The InFARM IT platform and system are designed to aid countries in gathering, analysing and effectively utilising their AMR data within the domains of food and agriculture, all geared towards national objectives.

Initially, InFARM will focus on hosting AMR data from priority bacterial species significant to public health, animal health and indicator bacteria from animals and food sources.

Implementing InFARM will adhere to international standards and recommendations set forth by the Codex Alimentarius and WOAH. The IT system will support countries that are eager to share their AMR data for global surveillance purposes, also serving as the conduit for integrating data from the food and agriculture sectors into the Quadripartite Global Integrated System for Surveillance of Antimicrobial Resistance and Antimicrobial Usage.

Reducing need for antimicrobials in agrifood systems

FAO is also launching an action-oriented 10-year global initiative called Reduce the Need for Antimicrobials in Agrifood systems (RENOFARM). The initiative involves the entire production chain in a joint effort to strengthen capacity at the primary production level.

RENOFARM aims to directly contribute to better production, nutrition and the environment by making farms healthier and more sustainable.

This initiative will contribute toward countries’ agrifood systems transformation through the provision of comprehensive support in the implementation of good production practices, health and vaccination programs, biosecurity measures and antimicrobial alternatives.

The ultimate goal is to reduce the need for antimicrobials and promote their responsible use when needed.

Supporting implementation of national action plans on AMR

Challenges persist within countries when implementing national action plans (NAP) on AMR. These challenges include the need to comprehensively incorporate all aspects of the food and agriculture sectors, establishing effective monitoring and evaluation mechanisms for the NAPs and timely updating NAPs that are set to expire.

Recognising these key challenges, FAO’s sector-specific work on AMR also focuses on developing global tools for adaptation and use at regional and country levels and providing
tailored technical support for implementing countries’ national AMR action plans. Major tools and initiatives include:

- As many as 23 countries across the regions have used the Progressive Management Pathway for Antimicrobial Resistance (FAO-PMP-AMR) to develop and / or enhance the implementation of national AMR action plans through a stepwise approach to the management of antimicrobials and AMR response in agrifood systems
- The FAO Assessment Tool for Laboratories and Antimicrobial Resistance Surveillance Systems (FAO-ATLASS) was used in 28 countries in 2021 and 2022
- Implementation of international standards such as the Codex Alimentarius texts by FAO and WHO related to foodborne AMR
- FAO has directly supported AMR-related activities in the food and agriculture sector in 47 countries in Africa, Asia, Europe, Latin America and the Caribbean.

Preventing antimicrobial resistance together

Established by the quadripartite, the AMR Multi-Stakeholder Partnership Platform is an inclusive, international and multi-stakeholder forum. Bringing together relevant stakeholders across the human, animal, plant and environment sectors to assist in preserving antimicrobials as lifesaving medicines for all organisms and ensuring their responsible use under a One Health approach.

The platform is instrumental in building and promoting a shared global vision of AMR and catalysing a global collective engagement and action around shared priorities on AMR. It will help define targets and activities to inform bold and specific commitments at the United Nations General Assembly High-Level Meeting on AMR in 2024 and the 2024 High-Level Ministerial Meeting on AMR.

As we observe World AMR Awareness Week in 2023, we must remind ourselves of the significance of each sector and the importance of working together to tackle AMR. The misuse and overuse of antimicrobials are the primary drivers of AMR. Therefore, adopting a whole-of-society and multi-sectoral approach is essential to address this global issue effectively.

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Natural livestock farming effective bottom-up approach to reduce antibiotic use in dairy sector

Crisis with AMR obliges dairy sector to look beyond maximising cattle productivity and focus on both milk quantity, quality

By Katrien van’t Hooft, M N Balakrishnan Nair
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In the world-wide quest for dairy modernisation, the focus on crossbreeding and productivity increase of dairy cattle has — besides enhanced milk production — also resulted in high use of agro-chemicals. The use of antibiotics for common cattle diseases, such as udder infection and diarrhoea, is widespread. This contributes to the global threat of anti-microbial resistance (AMR).

Natural Livestock Farming approach

Since 2014 farmers, livestock scientists and veterinarians from Ethiopia, Uganda, India and the Netherlands have joined forces under the umbrella of the Natural Livestock Farming Foundation (NLF).

This international network on knowledge development for livestock health is re-valuing time-tested methods, such as use of medicinal plants and strategic use of local breeds, to be applied in a modern context. NLF combines knowledge from various backgrounds including farmer knowledge, western veterinary science and ayurveda.

The foundation improves cattle health on basis of the NLF 5-layered approach (van’t Hooft et al., 2017) comprising:

- Appropriate management of animals, farm and soils
- Strategic use of local breeds, strategic crossbreeding
- Ethno-veterinary practices (EVP): use of herbs and natural products
- Food quality improvement and control
Better farm income through cost reduction and direct marketing

NLF core activities are action research, exchange of best practices, and training. The combination of bottom-up experimentation and international peer-to-peer exchange is additional to existing initiatives in the field of AMR control.

This opens up opportunities that more conventional livestock development programmes fail to unlock, providing opportunity for increased farm income, better child nutrition, food safety & security, as well as improved environment.

Results in smallholder dairy system

EVP as part of the NLF 5-layer approach is gradually being adopted, especially within countries with smallholder dairy farmers. The main example being India, the largest dairy producer in the world, based on 98 per cent zero-grazing smallholder dairy farmers with 2-5 cows.

Over the past decade, NLF India (a collaboration between GLOHMSIWA Research Labs Pvt Ltd and Trans Disciplinary University) has trained a total 30,000 farmers and 2,000 veterinarians on efficient use of herbs for cattle health, also known as EVP. (M.N.B. Nair, 2019)

Since 2017, the method has been adopted by the National Dairy Development Board. Through an online reporting system, the empirical data of more than 556,000 cases of 30 bovine diseases cured with herbal medicine were recorded. An overall average cure rate of 82 per cent, as well as an 87 per cent reduction of antibiotic use were registered within two years after the training.

NLF in Ethiopia (headed by Ethiopian Society of Animal Production ESAP), implemented an action research based on the NLF approach in two zero-grazing smallholder dairy communities.

Experts from NLF India headed a training on the use of medicinal plants (mainly kitchen herbs), while organisations collaborating with NLF Netherlands guided training on laboratory skills and calf management.

In two years, the approach has shown significant improvement in milk quality (eight per cent antibiotic residue reduction) and quantity (over 50 per cent increase), farm income (33 per cent increase), while calf mortality was reduced by 60 per cent.

Average costs for cattle health were reduced by 20 per cent. The outcomes of this pilot will have a bearing in supporting the Ethiopian Ministry of Agriculture in improving milk quality and to scale up the strategy into various dairy programmes.

The initial focus of NLF in Uganda (headed by the Lake Mburo Farmers Cooperative Society) was on natural control of ticks and tick-borne diseases among smallholder ranging cattle.

A herbal recipe based on local plants was developed by experts from NLF India and tried out in 2017-2018. In recent years the society has also focused on diversifying farm activities including value addition and local marketing of dairy products.
Results in large-scale dairy

Since the start of NLF in the Netherlands in 2015, around 400 farmers and 50 veterinarians have joined the activities. The antibiotic use for mastitis in the dairy sector used to be high, with dry cow treatment a common practice.

Since 2014, a one-to-one relationship between farmers and veterinarians on the use of antibiotics was enforced by the government, with mandatory (national) registration of antibiotic use. As a result, the use of antibiotics in the total livestock production systems was reduced to around 70 per cent compared to 2009, though the decrease is now stagnating.

In the Dutch dairy sector, increased use by farmers of ready-made natural products was one of the major changes for mastitis prevention and cure. Moreover, farmers started to reintroduce herbs in the cattle feed and ray-grass monoculture grasslands.

This exposed the lack of knowledge among farmers and veterinarians, both about herbal grassland management and the safety of herbal products. Since 2018, NLF in the Netherlands has trained farmers and veterinarians on the safe use of herbal products and herbal grassland management. The Dutch government has invested in the spread of knowledge on natural remedies via so-called Barn-books (Groot et al., 2021).

EVP for improving milk quality

In dairy development, the main focus has been on maximising cattle productivity and milk quantity. At this point in time, the crisis with AMR obliges the sector to look beyond this and focus on both milk quantity and milk quality. Meanwhile, knowledge and skills about practical ways to reduce the use of antibiotics at farm level without harming cattle health and wellbeing are lacking.

The strategic collaboration headed by NLF has brought about a road map on improving cattle health and milk quality. Now that proof of concept about the NLF approach including EVP is available it is time for further upscaling into mainstream dairy policies, extension and education.

For this, NLF is reaching out to non-profits, governments, research institutes and funding agencies, while organising webinars, field level pilots and international exchanges.

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FAO’s biosecurity protocol can help create healthy farms with less antibiotic use

The three-zone biosecurity initiative by FAO was originally launched in 2013 to contain avian flu outbreaks

By Satya Sivaraman

The Food and Agriculture Organization (FAO) of the United Nations has created a three-zone biosecurity protocol, which has the potential to be a crucial tool in combating antimicrobial resistance (AMR) resulting from the use of antibiotics in animal agriculture. The initiative has helped egg farmers in Indonesia grow their income while reducing the need for antibiotics.

The World Antimicrobial Resistance Awareness Week takes place from November 18-24 every year.

Adopting the protocol was one of the best decisions taken by Ievan Purnateja, a medium-sized egg producer in the Indonesian province of Lampung, to help maintain very high hygiene standards on his farm. Purnateja now harvests healthy eggs regularly, which are in high demand among consumers.

The FAO’s three-zone biosecurity initiative was originally launched in 2013 to contain an outbreak of the deadly avian flu. The avian flu pandemic killed hundreds of thousands of birds and led to millions of dollars in losses for farmers all over Southeast Asia.

The protocol aimed to reduce infection on poultry farms by ensuring proper isolation, traffic control, cleaning and disinfection. Under the protocol, the livestock area on the farm gets divided into three zones, namely red or high risk, yellow or moderate risk and green or low risk.
Vehicles and footwear from outside the farm are placed in the red zone. In the yellow zone, special footwear is used and farm workers must take a shower and wear protective clothing. When they enter the green zone, they are required to wear special footwear and sanitise their hands and feet before coming into contact with the birds.

“People’s awareness about healthy food is very different from a couple of decades ago. They were ignorant in the past, but now they demand very high standards of hygiene in their food products,” Purnateja said.

Implementing the biosecurity protocol for his flock of over 80,000 chickens was worth it, said the egg farmer. “Though it required investment in new facilities and materials, given their benefits, the three-zone biosecurity measures are not that expensive after all,” he added.

Improving hygiene practices using the FAO guidelines also helped Purnateja obtain a veterinary control number, also known as NKV certification, issued by the Indonesian Ministry of Agriculture. The NKV certification is a stamp of food quality and safety and essential for accessing new, lucrative markets, including domestic supermarkets and export markets.

Since 2005, NKV certification has been mandatory for slaughterhouses and food distribution businesses in Indonesia.

The NKV certification ties in well with the FAO biosecurity initiative. Currently, poultry farms in 14 provinces are implementing the FAO protocol. The key to its popularity is the significant increase in profits for small and medium farmers, who often do not have the facilities of large factory farms.

Indonesia’s poultry population has increased steadily in the last few decades. It supplies 65 per cent of all animal protein and employs 10 per cent of the national labour force. Production of poultry meat in Indonesia increased from 79,301 tonnes in 1972 to 3.89 million tonnes in 2021, growing at an average annual rate of 8.82 per cent.

While the FAO team provides the technical inputs, the investment in building the infrastructure required, obtaining protective equipment and other materials is borne by the farmers.

“We, in Indonesia, have been doing cost effectiveness studies and we found out that if you do three-zone biosecurity, there is a positive return on investment,” says Luuk Schoonman, team leader of the FAO Emergency Centre for Transboundary Animal Diseases (FAO-ECTAD), Indonesia.

An FAO study of broiler production, conducted over a two-year period, found seven farms that adopted the three-zone biosecurity measures earned an additional $45 for every 1,000 birds. In the same period, the income in four control farms was reduced by $33 per 1,000 birds.

This unique partnership between FAO, government agencies, private industry and farmers also has a special public health benefit — a reduction in the use of antibiotics in the poultry industry.
“Farmers who implement the three-zone biosecurity protocol have been able to reduce antimicrobial use” said Alfred Kompodu, technical officer, FAO, Indonesia.

A study by the Indonesian Ministry of Agriculture in Semarang district, Central Java province in layer farms found a 42 per cent reduction in antimicrobial use in the FAO-assisted poultry farms.

The study, looking into reducing antibiotic use in layer farms by implementing three-zone biosecurity, was based on data from two farms, each housing around 25,000 birds, with one implementing the three-zone biosecurity measures while the other did not.

There are no formal estimates nationally, but AMR is thought to be high and on the rise in the country. Antimicrobial use is quite prevalent in the livestock production sector, especially poultry.

In 2017, the Directorate General of Livestock and Animal Health Services and FAO-ECTAD conducted antimicrobial use surveys to gain insights on antibiotic use patterns in poultry production. The survey found that most farmers (61 per cent) believed that antibiotics were a necessary component in the successful breeding of broilers. The majority (81.4 per cent) of poultry farmers still used antibiotics for prophylaxis, 30.2 per cent for medical treatment, and 0.3 per cent as growth promoters.

According to Schoonman, the FAO three-zone biosecurity project in Indonesia could be a simple, but effective model for lowering the use of antibiotics in poultry farms. This is especially true when combined with food safety certifications such as NKV that attract farmers to adopt biosecurity measures voluntarily.

More research, with a larger sample size of birds and farms, is required to fully validate the link between the FAO protocol and lowered use of antimicrobials. With that done, the three-zone biosecurity model — which is low cost, easy to implement, increases production and reduces infection — can be replicated by poultry farmers, not just in Indonesia’s neighbourhood but in low- or middle-income countries across the globe.

Satya Sivaraman is a communication advisor to ReAct Asia-Pacific, which is part of a global network of academic institutions and civil society groups working on antimicrobial resistance.
The link with climate change, water & why we need to incentivise measures against antimicrobial resistance

Many countries now have national AMR action plans, but implementation remains vastly different

By Iris Panorel, Jakob Schabus
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The World Antimicrobial Resistance Awareness Week takes place from 18-24 November, 2023. Antimicrobial resistance (AMR) is ranked as one of the biggest global health threats. What is behind the rise of AMR, how does it connect to water, and what can we do about it? Here are the answers.

AMR is a silent and slowly emerging pandemic. Behind it is the ability of microbes to evolve and develop defense mechanisms against antimicrobial agents such as antibiotics and antivirals. As a result of this process, antimicrobials become less effective and infections harder to treat.

This is particularly dangerous for patients with a weakened immune system, such as those battling cancer or undergoing surgery, who can be at risk of infections.

Over time, AMR has become one of the biggest global health threats for humanity. According to the United Nations Environment Programme (UNEP), AMR could push 24 million people into extreme poverty in the next decade and shave off trillions of dollars of GDP if we do not take the right measures. How did we end up in this situation?

Drivers behind AMR

While AMR is a natural process, there are factors that accelerate antimicrobial resistance. Some of them are well-known such as the use, overuse and misuse for human and animal health. This entails the lax prescription of medicine through some medical professionals, or the risk posed through patients that do not take all prescribed antimicrobials, which can lead to infectious microbes surviving and developing resistance to the medicine.

A large part of the challenge lies with the agricultural industry. Approximately 70 per cent of global antibiotic sales go to it. The medicine is used for animals raised for food with the goal of treating or preventing infections or increasing the body mass of livestock.

Although the European Union has banned the practice of routinely feeding antibiotics to animals, other parts of the world continue to do so.

What is less known is the close connection among climate change, water and AMR. In the last three to five years, we started to really understand that climate change accelerates the development and spread of AMR.

Climate change is experienced primarily through too much, too little, or too dirty water. All three can worsen AMR as lack of access to clean water in drought affected areas as well as the exposure to polluted flood waters lead to increased infection rates. This means the start
of a vicious cycle. Increased infections are followed by a rising use of antibiotics, which increases the probability of new and higher levels of AMR.

Finding solutions is complex

The current crisis is exacerbated by the fact that the big players in the pharma industry are increasingly abandoning antibiotics. The costs of producing a new antibiotic are massive. Potential revenues through sales are highly uncertain.

One reason for this is that doctors try to avoid prescribing newly developed antibiotics, unless a patient is at an extremely high health risk from an infection, to help delay AMR. At times this requires a difficult question of conscience for medical practitioners who need to decide between using new antibiotics which could accelerate AMR or old ones which might in some cases not be sufficiently effective to treat an infection.

This is not the only challenge for producers. In many countries, government agencies want to keep the prices for antibiotics low.

Further, many patent periods for antibiotics have expired. This allows new manufacturers to take over the market. The increased competition drives the prices down. This leads to another negative spiral as many of the smaller manufacturers only have marginal profits and would not have the capacity to invest in sufficient wastewater management.

Oftentimes, the result is pollution through antibiotics in the surrounding area of the production compound, a local problem with global effects.

Enhancing cooperation

The fight against AMR is a challenging one but there are steps that can be taken. To make meaningful progress actors across regions and sectors need to be part of the solution. A strong openness to work with people from different backgrounds and sectors to connect knowledge, capacities and resources both from the Global North and the Global South is needed.

The responsibility lies not only with medical doctors and veterinarians who prescrib, and the patients who consume, but also with hospitals, municipal wastewater plants and producers that have large amounts of antimicrobials in their waste.

At the same time, governments need to set up and implement regulations, provide financing and enable stakeholders to work together.

Providing incentives for good practices

Stockholm International Water Institute (SIWI) has been working with pharmaceuticals in the environment with a focus on antibiotics for the past five years. Aside from governments, SIWI’s prime target group is the manufacturing industry as well as procurers with the dedicated aim to minimise emission of antibiotics through the manufacturing process, improve policies and reduce the spread of AMR.

In the recently published Framework, SIWI defined factors and criteria for responsible manufacturing to significantly slow the spread of AMR. The criteria suggest pathways for the procurers and regulators to provide incentives in the form of financial security or an
improved reputation to manufacturers who can demonstrate that they are producing antibiotics responsibly.

Many countries now have national AMR action plans, but implementation remains vastly different. The World Health Organization has recently released a package of interventions to help governments in implementing a more comprehensive response to AMR through a people-centered approach. This is part of a larger positive trend that has started in recent years.

The conversation across sectors and actors is evolving and attention to the policy field is increasing. Now it is time to build on the momentum and slow the global spread of AMR together.

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Way forward for pharma companies to ensure antibiotics manufacturing doesn't drive resistance

The risk of AMR posed by the release of antibiotic manufacturing waste can be prevented

By Martijn van Gerven
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Antibiotics are a cornerstone of modern medicine, enabling humans to fight off a huge variety of dangerous infections, and it is critical that companies produce antibiotics in quantities enough to meet the world’s needs.

Unfortunately, the process of manufacturing these lifesaving medicines can actually contribute to antimicrobial resistance (AMR), which is a multifaceted and growing challenge that threatens the efficacy of antibiotics in the face of rising drug resistance.

The overuse and misuse of antibiotics are well-known drivers of AMR, as is lack of access to appropriate antibiotics. However, the risk of AMR posed by the release of antibiotic waste into the environment is often overlooked.

Put simply, if waste generated from antibiotic manufacturing contains high levels of active pharmaceutical ingredients (APIs) when discharged into rivers and waterways, it poses a serious risk to the emergence and spread of AMR and can cause environmental harm. But by manufacturing responsibly, pharmaceutical companies can prevent this risk.

Moreover, pharmaceutical companies are some of the largest players across antibiotic manufacturing supply chains, and the steps they take to prioritise responsible manufacturing practices can have a transformative impact across these supply chains.

AMR Awareness Week is observed from November 18-24 every year.

Three clear ways

Through our dedicated AMR Programme, the Access to Medicine Foundation tracks and scores the efforts of major pharmaceutical companies to address AMR in the AMR Benchmark, including assessing whether they are engaging in responsible manufacturing practices for their antibiotics and antifungals.

While progress in this area has been identified since the first Benchmark was published five years ago, our research showed that significant gaps remain. For this reason, earlier this year we published a report focused specifically on the topic of responsible manufacturing, setting out clear, research-based solutions that pharmaceutical companies can deploy to enable industry-wide progress.

Start at the source: First, companies need to implement effective wastewater management methods to ensure the concentration of antibiotics in their wastewater does not trigger resistance. Currently, it is common practice for companies to assess the concentration of antibiotics in a river, after they have released their manufacturing wastewater. However,
this means that the estimated concentrations will be diluted. Moreover, bacteria are first exposed to antibiotics in wastewater before it is released. Going forward, companies can ensure that the concentration of antibiotics in wastewater that leaves a factory complies with safe discharge limits before releasing it into the environment.

**Promote practices more widely:** As a second area of focus, companies can utilise their unique positions in the antibiotic supply chain to ensure that suppliers of APIs also manufacture responsibly. Given that there is often a heavy reliance on a limited number of suppliers of critical drugs, working with suppliers to help them adopt responsible manufacturing practices can help drive wider industry change without jeopardising the supply of antibiotics to patients.

**Share information to drive progress:** Finally, companies can publicly disclose how they are managing antibiotic waste. Sharing information about where, and how much, antibiotic waste is released into local rivers is key to understanding where AMR risks are located and will help to hold individual companies accountable on their commitments.

**Path forward**

In tackling the various drivers of AMR, limiting the release of antibiotic waste is a clear way for pharmaceutical companies to prevent drug resistance — or at the very least ensure they do not contribute to the problem. Encouragingly, the best-in-class examples identified in our report do show that progress is possible. But for wider impact to be achieved, more companies need to act.

Beyond curbing AMR, companies that do proactively develop and scale responsible manufacturing practices can safeguard their business for the future — especially considering how the global policy and procurement landscapes are shifting. Governments, regulators, procurers, and investors are focusing more keenly on the risks of AMR from manufacturing and are increasingly expecting companies to demonstrate responsible manufacturing practices.

Aside from signs that regulation aimed at reducing AMR risk from manufacturing could be introduced in certain countries and regions, procurers are also rewarding companies if they manufacture responsibly and adhere to environmental standards. In Norway, for example, companies that perform best in limiting AMR risks from manufacturing, are already winning national tenders for antibiotics.

Some companies have shown that they are already proactively and voluntarily strengthening their efforts. More companies need to seize opportunities for progress, not only to fulfil their vital role in preventing AMR, but also to ensure they are at the forefront of a global health landscape that is increasingly paying attention to drug resistance and its drivers — including antibiotic waste from manufacturing.

*Martijn van Gerven is research coordinator, Access to Medicine Foundation.*
Behavioural, organisational and environmental aspects are vital for containing resistance

Problem underpinned by complex drivers and behaviours; multisectoral and multidimensional efforts required

By Venkataramanaiah Saddikuti, Ranga Reddy Burri
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Antimicrobial resistance (AMR) is among the top 10 global threats to human health, according to the World Health Organization (WHO). AMR could push over four million people into poverty and cause up to 10 million deaths per year by 2050, a United Nations Environment Programme (UNEP) study estimated.

Studies in the journal The Lancet and by the WHO on AMR and its burden have referred to it as a slow pandemic. The containment of AMR is critical for achieving UN-mandate Sustainable Development Goals (SDG). It requires multisectoral efforts and multidimensional approaches that include organisational, behavioural and environmental aspects, particularly in low- and middle-income countries.

The AMR problem is underpinned by complex drivers and behaviours, including environmental factors. From an environmental perspective, the main contributors to AMR include pollution from agriculture, pharmaceutical health and other sectors. Action is necessary to reduce the emergency transmission and spread of bacteria strains and instances of AMR.

The impact of pollution on AMR was also pointed out by UNEP Executive Director Inger Andersen, who said:

Pollution of air, soil and waterways undermines the human right to a clean and healthy environment. The same drivers that cause environment degradation are worsening the AMR problem. The impacts of AMR could destroy our health and food systems

The concept of One Health focuses on health, agriculture and environmental protection. One method of containing it is to manage the entire chain of antibacterial agents and AMR.

Environmental pollution is mainly caused by a lack of strict control over the disposal of health, agriculture and pharmaceutical waste, particularly in low- and middle-income countries. Controlling pollution sources like poor sanitation, sewage and community and municipal waste is key.

One Health framework suggested improved water management, governance, planning and regulatory and legal frameworks at the national level. It also suggested international standards for microbiological indicators, investments in AMR containment and funding for sustainable development.

For example, Delhi-National Capital Region (NCR) is suffering from severe air pollution, which is causing health issues and affecting economic development. Governments are
taking precautions like banning the entry of old vehicles into cities like Delhi, banning the burning of agriculture residues in neighbouring regions / states, etc.

India proposed a national action plan for controlling AMR in 2017 in line with the One Health framework and an additional aspect on socioeconomic conditions like education and awareness among the public. The national action plan focused on both human and non-human sectors and included the following:

- Control on excess use or misuse of antimicrobial agents in both human and animals
- Effective management of various wastes, like waste water from pharmaceuticals, municipal waste, hospitals and other sectors
- Improved management of livestock, agricultural manure and sludge
- Effective management of heavy metals, aquaculture
- Political commitment and innovative ideas from other sectors, like Swachh Bharat Abhiyan

China also responded to AMR containment by following WHO recommendations. The country’s action plan included the development of new drugs and technologies, the sale of antibiotics with prescriptions, the optimisation of surveillance, the rational use of antibiotics in both the human and animal sectors and professional education and public awareness about AMR.

The organisational dimension requires a focus on understanding the true picture across the country rather than a few selected locations/centres. It requires improvements to laboratory and training infrastructure and adequate and trained manpower. Quality standards are also required at all locations that cater to the growing needs of sectors such as health, agriculture, and pharma, all of which contribute to the growth of the AMR problem.

The involvement of government, private, and non-profit organisations in the fight against AMR is critical and urgent. Setting up adequate research and development and supply chains for optimal supply and use of antimicrobial drugs is critical from an organisational standpoint.

Current advancements in information and digital platforms can serve as cost-effective mechanisms for addressing AMR containment. Tamil Nadu and Kerala in southern India are the best examples of establishing health infrastructure and ensuring an adequate supply of essential drugs in public health facilities. WHO has recommended such efficient models for other countries to address health care delivery.

One of the most difficult aspects of not only AMR containment but also other aspects of society is behavioural change. Health-related behavioural changes have become critical in both policymaking and large-scale, sustainable implementation.

It is critical to develop and implement appropriate strategies for behavioural changes aimed at individuals and organisations. Doctors and other healthcare professionals, for example, can educate individuals on good health behaviours such as sanitation, food, and other habits, as well as the effects of antimicrobial drug overuse and misuse.

It has also been observed that using children as change agents for good health behaviours has worked effectively in a number of countries; therefore, it is strongly recommended that
these strategies be used at the national level for countries such as India and China, among others.

Conducting awareness programmes alone will not be sufficient to achieve the end goal of containing AMR. Designing and implementing appropriate / contextual behavioural change strategies based on cultural, socioeconomic, and environmental factors is critical.

India can learn from successful programmes like polio eradication / vaccination programme and Swachh Bharat Abhiyan wherein the Prime Minister of India appealed to citizens and led the initiative himself along with all the key stakeholders of the country. Community engagement is vital for the success of any such large-scale programme and a similar approach can help India contain AMR effectively.

An integrated approach is required from an environmental standpoint to control contamination from various sectors such as pharma, agriculture, health, food, and others. Strict regulatory controls and coordinated interventions at all levels are required. Innovations such as public-private partnerships for national environmental management are a tried and true method.

Appropriate policy changes, the establishment of standard operating procedures for monitoring and controlling various AMR measurables, and the large-scale, long-term engagement of various stakeholders and communities can all help in the fight to contain AMR.

Venkataramanaiah Saddikuti is a professor of operations and supply chain management at IIM Lucknow and Fulbright scholar to USA in healthcare management; Ranga Reddy Burri is President – Infection Control Academy of India and Honorary Professor – School of Medical Sciences, University of Hyderabad
Pharma must rise to the challenge as stewards of public health

Being in the pharmaceutical field, the mantle of responsibility falls upon us to forge ahead in the relentless pursuit of solutions to the daunting challenge of AMR.

By Manjit Singh
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In the relentless battle against antimicrobial resistance (AMR), antibiotic producers find themselves at the forefront, facing an arduous task that demands unwavering commitment and innovative solutions.

With a decade of experience in the field, it is evident to me that the threat of AMR has escalated exponentially, necessitating a comprehensive and collaborative response from the pharmaceutical industry.

The escalating crisis: Sleeping pandemic

As we navigate the intricate landscape of AMR, statistical data paints a stark reality. According to recent research by The Lancet journal, AMR caused an estimated 700,000 deaths annually worldwide in 2019. India, with 297,000 deaths attributable to AMR in 2019, topped this list.

In India, most research on the Musi river and industries surrounding it in Hyderabad, Telangana indicated a deep linkage between AMR and antibiotic emissions from manufacturing.

Work on the Sirsa rivulet in the Baddi-Barotiwala-Nalagarh pharma cluster in Himachal Pradesh also flagged a similar linkage of AMR with industry.

Reports about antibiotic pollution in the media have shaken industry, governments and other stakeholders to contemplate and act.

Challenges, barriers and progress

The antibiotics industry faces the formidable challenge of preserving antibiotics efficacy and ensuring their supply chain. AMR poses a huge business and reputational risk.

A major chunk of industry is in a state of confusion given the magnitude of the challenge which comprises paucity of understanding, scientific knowledge, clear policy, methodologies for risk assessment, wastewater treatment technologies, infrastructure investments, wastewater treatment cost impact and eventually, sufficient margins to survive and compete.

However, the sector has diligently engaged with stakeholders to build approaches and continue optimistic messaging inside the antibiotics supply chain.
For instance, key players signed the United Nations General Assembly Declaration To Combat AMR and helped in the formation of Antimicrobial Resistance Industry Alliance (AMR IA). Pharmaceutical Supply Chain Initiatives (PSCI) have embraced AMR as a priority in their agenda.

Innovative approaches: A beacon of hope

Amid the challenges, there is a glimmer of hope as the pharmaceutical industry embarks on pioneering initiatives to tackle AMR. Collaborative industry efforts are exploring innovative avenues to reduce antibiotics emissions, such as high isolation yields, recovery of antibiotics from mother liquor, innovative decontamination methods and efficient wastewater treatment technologies to eliminate residual antibiotics.

The pioneering work of AMR IA and British Standards Institute (BSI) resulted in the release of the first Industry AMR standard in 2022 and AMR certification in 2023 for sustainable manufacture of antibiotics.

AMR standard provides solid guidance and direction by setting safe discharge limits known as Predicted No Effect Concentration (PNEC) for wastewater, Risk Quotient threshold limit, methodologies for risk assessment by deploying mass balance and / measurement through testing, measures to mitigate to avert AMR risk. The adaptation of AMR standard and certification by antibiotic manufacturers has tremendous potential to ameliorate the prevailing situation.

Global initiatives: Acting as pressure point to industry

Collaborations and initiatives are emerging in the direction of the One Health Approach programme launched by the World Health Organization, bringing together all stakeholders from manufacturing, healthcare, agriculture and authorities.

Some of the pathbreaking developments will discourage unsustainable manufacturing of antibiotics both, Active Pharmaceutical Ingredients (API) and Finish Dosage Forms. Unprepared manufacturers will be caught by surprise, with a sizeable impact on their operations in wake of the following developments.

- Introduction of AMR criteria by insurers for medicine procurement tenders
- WHO guidance to evaluate AMR during inspections
- Five Nordic countries and UK proposed incorporation of AMR criteria for antibiotics procurement
- EU pharma legislation revision (under approval) included environmental criteria including AMR for supply of medicines
- Inclusion of residual antibiotics limits in the proposed Environment standard amendment 2020 by Indian Ministry of Environment, Forest and Climate Change. Although these limits are withheld in the approved amendment in 2021, ministry is contemplating to include in future
- AMR IA member companies’ commitment to implement AMR standard and AMR certification
- PSCI sustainability principles, many other platforms and NGO focus at antibiotics mfg. and their linkage with antimicrobial resistance
Bold steps ahead: Call to action to build an impactful momentum

As we stand at the precipice of a critical juncture in the fight against AMR, it is evident that bold and decisive action is paramount. The pharmaceutical industry must collectively rise to the occasion, not merely as purveyors of drugs but as stewards of public health. The present scale of efforts and industry preparedness at ground level is insufficient to tackle the AMR menace.

In conclusion, the industry associations, promoters, professionals, and authorities must act in tandem, include AMR into their business strategy, build actions plans, allocate budget for initiatives and targets.

It is paramount to have a carrot-and-stick policy in place to incentivise sustainable antibiotics suppliers. India, being a major player in the global pharmaceutical supply chain, must act proactively and with conviction to maintain leadership and reputation.

Being in the pharmaceutical field, the mantle of responsibility falls upon us to forge ahead in the relentless pursuit of solutions to the daunting challenge of AMR.

Manjit Singh is founder & AMR expert at Sustainability Edge Consulting. He is former global director- Corporate Sustainability Centrient Pharmaceuticals, former chair – PSCI and member of AMR IA
Combating AMR in European Union through a One Health approach

Today, one in five bacterial infections in Europe is caused by a pathogen that is resistant to antibiotics

By Kris De Smet

Antimicrobial resistance (AMR) causes more than 35,000 deaths and costs European Union (EU) / European Economic Area countries around €11.6 billion ($12.66 billion) each year. The AMR health crisis can no longer be called a silent pandemic. It is a very real and present threat throughout the globe. We need to act right away.

This is why fighting AMR with a One Health approach is a firm priority of the European Commission and the EU Member States now more than ever. The good news is that we don’t need miracles to change things.

The World Antimicrobial Resistance Awareness Week takes place from November 18-24 every year.

New data released by the Organization for Economic Cooperation and Development (OECD) showed that every European country needs to spend just €3.4 per capita every year on a mix of hospital and community-based AMR interventions. This could prevent more than 10,000 deaths, avoid over 600,000 new infections and save more than €2.5 billion for their health systems. Every Euro invested in prevention would bring nearly €3 in economic benefits. At the OECD level, this ratio goes up to 1 to 5.

Today, one in five bacterial infections in Europe is caused by a pathogen that is resistant to antibiotics. In about 10 years, nine out of 10 of hospital-acquired bacterial infections will be multi-resistant, if nothing is done. By 2035, it might be more dangerous to go to a hospital than to get treatment at home if we do not tackle AMR as a matter of urgency.

Events like European Antibiotic Awareness Day and World AMR Awareness Week certainly have their impact. But, unfortunately, these are not enough to reach the general public. Today 40 per cent of Europeans still think that antibiotics kill viruses.

For this reason, we must urgently raise awareness of AMR in Europe and across the world. Clinicians, healthcare professionals, veterinarians, and farmers must speak out about it because they are on the front lines of tackling it. AMR champions, such as public figures and celebrities who advocate for the fight against it, should also bring this to the public's attention. At the same time, we must also work to address misinformation and misconceptions about AMR.

Effective policy measures — human, animal and environmental — are needed to respond to the AMR challenge in the EU and globally. In June this year, EU health ministers agreed on an ambitious plan to step up actions to combat AMR through a One Health approach.

They agreed on several targets to be achieved by 2030. Most significantly, we are working to reduce the total consumption of antibiotics in humans by 20 per cent in the EU by 2030, compared to 2019. Such targets allow us to monitor and compare progress across EU countries and to adjust and intensify measures if necessary.
The EU also has clear goals to reduce the sales of antimicrobials for farmed animals and aquaculture by 50 per cent. Here, the European Union is making good progress. The 13th European Surveillance of Veterinary Antimicrobial Consumption report showed that by 2022, EU countries were over halfway to reaching this target. In addition, sales of antimicrobials for farmed animals and aquaculture fell by over 28 per cent in 2022.

However, targets alone are not enough. The EU is also undertaking a range of other actions, including enhanced monitoring and surveillance, better prevention and control measures, boosting research and development and incentives for innovation.

The European Commission’s proposal to revise the EU’s pharmaceutical legislation also puts forward specific solutions to stimulate the development of novel antibiotics, ensure access to existing ones and improve the prudent use of all antimicrobials.

On the veterinary side, in addition to the target, EU legislation also bans the use of antibiotics for prophylactic purposes or as growth promoters in certain farmed animals. The European Commission organises hands-on training sessions for farmers and veterinarians to raise awareness on the measures to fight AMR and we provide direct grants to EU countries to help them improve their data collection and reporting on veterinary antimicrobials.

On the environmental side, last year the European Commission proposed to strengthen environmental monitoring of AMR in ground and surface waters. Our pharmaceutical reform will extend the environmental risk assessment of medicines to cover antibiotic manufacturing.

Last but not least, the European Commission provides considerable financial support under EU funding programmes. For example, the EU is investing €50 million to support a new Joint Action on AMR early next year to help all EU countries tackle it through a One Health approach. This is in addition to €22 million to bring AMR countermeasures to the market and support Member States in their procurement.

Since AMR does not recognise national borders, we clearly need a global vision and response for it. This is what the European Commission is striving for in all international fora, as outlined in the EU Global Health Strategy. The European Commission is leading discussions at the G7 and G20, pushing for a global health agenda based on a One Health approach with AMR at its core. This is also at the heart of the EU’s position in the ongoing negotiations for the World Health Organization’s pandemic agreement.

In parallel, the Commission provides significant funding to low- and middle-income countries to support their AMR agendas, for example through projects on antimicrobial stewardship in hospitals in Sub-Saharan African countries and by supporting surveillance programmes and technology. The EU also cooperates with these countries on food safety and animal health, given that 10 per cent of the world’s population still eats food that was produced with contaminated water.

A major challenge for 2024 will be to make the upcoming United Nations high-level meeting on AMR action-oriented and not simply declaratory. AMR is a global problem that needs global solutions. It is only by acting together in a One Health approach that we will curb its tide.

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